

REMARKS

Claims 1-7 and 62-64 are pending and under examination. Claims 1, 2, and 6, have been amended. Claim 64 is new. Support for the amendment to claim 1 can be found, e.g., at page 9, lines 15-25; and page 10, lines 21-25, of the specification. The amendment to claims 2 and 6 merely correct typographical errors. Support for new claim 64 can be found, e.g., at page 10, lines 22-23, of the specification. No new matter has been added.

Applicant timely filed an Amendment in Reply to the Office Action of March 23, 2004, on September 23, 2004, with a Petition of Extension of Time and the required fee. The Examiner mailed a Notice of Abandonment on September 30, 2004. In telephone conferences with a colleague of the undersigned on October 19, 2004, the Examiner acknowledged that the Notice of Abandonment was sent in error. He further stated that he would note the rescinding of abandonment in the next Office Action rather than send a notice of rescinding of the abandonment. In the Office Action mailed January 26, 2005, the Examiner did not note that the abandonment was in error. Applicant respectfully requests that the Examiner note in the next Office Action that the abandonment was in error and was formally rescinded.

Rejections Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 1-7 and 62-63 were rejected as lacking written description. The Examiner stated

...CD44 polypeptides which are "at least 95% identical to SEQ ID NO:1 or to a sequence of a CD44 isoform arising from alternative splicing", "CD44H isoform" and "CD44R2 isoform" do not meet the written description provisions...[T]he HECA-452 antibody binds sialylated carbohydrate epitopes on various molecules and tissues...and is not restricted to CD44 polypeptides-or to KG1a/CD44H or CD44R CD44 isoforms...[T]he specification appears to indicate that there are multiple isoforms of CD44 by disclosing there is a "standard or hematopoietic isoform of CD44". Are there non-standard forms of CD44H and was applicant in possession of all these forms?...A person of skill would not know which sequences or structural elements are essential, which sequences or elements are non-essential, and what particular sequence lengths identify KG1a

CD44/CD44H/CD44R2 featured by the claimed invention. In the absence of structural characteristics that are shared by members of the genus of featured KG1a/CD44/CD44H/CD44R2 isoforms; one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. (emphasis in original)

This rejection is traversed. Applicant has amended the claims to advance prosecution and reserves the right to preserve broader claims in a continuation application. The claims are directed to preparations of a substantially purified glycosylated CD44 polypeptide comprising an amino acid sequence encoded by a nucleotide sequence comprising exons 1-5, 16, 18, and 20 of a human CD44 gene, wherein the CD44 polypeptide is a human CD44H isoform, a human CD44R1 isoform, or a human CD44R2 isoform, wherein the glycosylated CD44 polypeptide binds to an antibody having the binding specificity of monoclonal antibody HECA-452, and wherein the preparation comprises less than 30% of a polypeptide other than the glycosylated CD44 polypeptide.

The Examiner stated that "CD44H isoform" and "CD44R isoform" are not adequately described, e.g., because "[a]lthough page 10, paragraph 3 of the specification discloses a CD44R2 isoform, the actual structure of said CD44R2 isoform is not readily apparent." The polypeptide structures of the CD44 isoforms recited in the claims are supported by description in the specification and the art. The claims provide that these isoforms are encoded by a sequence comprising exons 1-5, 16, 18, and 20 of a human CD44 gene. Information which is well known in the art need not be described in detail in the specification. MPEP 2163.II.A.2. The sequences encoded by exons 1-5, 16, 18, and 20 of human, and of CD44H, CD44R1, and CD44R2 isoforms were known in the art at the time the present application was filed. One of ordinary skill would recognize this. Furthermore, the specification describes features of various isoforms. For example, it provides that CD44H (also known as CD44S) expresses exons 1-5, 16, 18, and 20 of the CD44 gene (specification, page 10, lines 22). The size, domain structure, and sites for glycosylation on this isoform are also discussed, e.g., at page 10, lines 22-31, of the specification. The Examiner questioned whether non-standard forms of CD44 were known. Non-standard forms such as CD44R1 and CD44R2 isoforms are described, e.g., on page 10,

lines 21-25. The polypeptide structure of a CD44R1 isoform is provided by SEQ ID NO:1 (page 10, table 1). Furthermore, as discussed in more detail below, the sequences of CD44R and CD44H isoforms are encompassed within the CD44R1 sequence of SEQ ID NO:1. The knowledge of one of skill, combined with Applicant's disclosure, provides ample description of the CD44 polypeptides recited in the claims.

The Examiner stated that the specification lacks description for polypeptides comprising an amino acid sequence "at least 95% identical to SEQ ID NO:1" or to a sequence of a CD44 isoform "arising from alternative splicing". While Applicants disagree with this assertion, these terms have been removed from the claims to advance prosecution.

The Examiner alleged that the claimed compositions lack description because the HECA-452 antibody binds sialylated carbohydrate epitopes and is not restricted to CD44 polypeptides. It is correct that the HECA-452 antibody is not specific for CD44 polypeptides. However, the polypeptides of the claimed compositions are limited to polypeptides encoded by a sequence comprising exons 1-5, 16, 18, and 20 of a human CD44 gene and that express HECA-452-reactive epitopes. These two features are to be considered together as part of the description of the claimed compositions. HECA-452-reactive polypeptides which are not CD44 isoforms do not fall within the claims.

It was also stated that the reliance on the disclosed examples of CD44 isoforms do not support description because the claims do not recite all of the relevant identifying characteristics such as structure or other physical and/or chemical characteristics that distinguish the claimed polypeptides from the genus of CD44 isoforms. The claimed compositions recite both polypeptide structure (i.e., amino acid sequences encoded by a sequence comprising exons 1-5, 16, 18, and 20 of a human CD44 gene) and a limitation which is both structural and functional in nature (i.e., binding to an antibody having the binding specificity of monoclonal antibody HECA-452). The claimed compositions also require that the preparation include less than 30% of a polypeptide other than the glycosylated CD44 polypeptide. This combination of characteristics distinguishes the claimed compositions.

Applicant respectfully requests withdrawal of the rejection of claims 1-7 and 62-63 as lacking written description.

Rejections Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 1-7 and 62-63 were rejected as lacking enablement for the claimed compositions. The claims have been amended to recite preparations of a substantially purified glycosylated CD44 polypeptide comprising an amino acid sequence encoded by a nucleotide sequence comprising exons 1-5, 16, 18, and 20 of a human CD44 gene, wherein the CD44 polypeptide is a human CD44H isoform, a human CD44R1 isoform, or a human CD44R2 isoform, wherein the glycosylated CD44 polypeptide binds to an antibody having the binding specificity of monoclonal antibody HECA-452, and wherein the preparation comprises less than 30% of a polypeptide other than the glycosylated CD44 polypeptide.

As discussed above with respect to written description, Applicant describes the polypeptide structures in the claimed genus. As the Examiner acknowledged, the specification is enabling for a KG1a/CD44 isoform expressed on normal human hematopoietic progenitor cells and leukemic blasts. Applicant has enabled other isoforms as well. The polypeptide structures of these isoforms are known. The specification discloses methods for identifying polypeptides that fall within the claims, e.g., by employing anti-CD44 and HECA-452 antibodies (as described, e.g., in Example 4 at pages 42-45 of the specification). It would not require undue experimentation to express a polypeptide encoded by a sequence comprising exons 1-5 16, 18, and 20 of a human CD44 gene, to express glycosyltransferases that modify the expressed CD44 polypeptides, and to prepare the claimed compositions by isolating the expressed polypeptides, given that tools for preparing the polypeptides and isolating them are described in the specification and/or are known (see, e.g., page 26, line 21, to page 27, line 20, describing expression of nucleic acids encoding CD44 and glycosyltransferases).

Rejections Under 35 U.S.C. § 112, Second Paragraph (Indefiniteness)

Claims 62 and 63 were rejected as indefinite for failing to particularly point out and distinctly claim the subject matter Applicant regards as the invention. This rejection is traversed. Claim 62 is directed to the preparation of claim 1, wherein the polypeptide is a CD44H isoform. Claim 63 is directed to the preparation of claim 1, wherein the polypeptide is a CD44R2 isoform. The terms "CD44H" and "CD44R2" are not arbitrary protein names but are names of specific isoforms. CD44H is described in detail at page 9, lines 15-31. The specification provides that this isoform is encoded by exons 1-5, 16-18, and 20 of a CD44 gene (page 9, lines 18-20). The open reading frame includes 1482 base pairs of mRNA and translates into a polypeptide chain of approximately 37 kDa (prior to modification by glycosylation)(page 9, lines 22-24). The approximate number of amino acids in each domain is also noted (page 9, lines 26-28). Because the amino acid sequence of CD44H is known and that detailed structure of the isoform is characterized in the specification, the term "CD44H" as used in the claim is definite. Applicant also notes that the entire sequence of the CD44H isoform is contained within CD44R1 (SEQ ID NO:1). CD44R1 differs from CD44H by the insertion of a 132 amino acid region corresponding to residues 223-355 of SEQ ID NO:1 (see Dougherty et al., *J. Exp. Med.*, 174:1-5, 1991). The term "CD44R2" is similarly definite. As is known in the art, CD44R2 differs from CD44H by the presence of an insertion of an amino acid sequence. The entire sequence of CD44R2 is contained within SEQ ID NO:1. CD44R2 differs from SEQ ID NO:1 in that it lacks amino acids 224-293 of SEQ ID NO:1 (see Dougherty et al., *J. Exp. Med.*, 174:1-5, 1991). Applicant submits that the terms "CD44H" and "CD44R2" are definite as used in claims 62 and 63.

Rejections Under 35 U.S.C. § 102(b)

Sackstein et al.

Claims 1-7 and 62-63 were rejected as anticipated by as anticipated by Sackstein et al. (*Blood*, 89:2773-2781, 1997; "Sackstein") as further evidenced by Dimitroff et al. (*J. Biol. Chem.*, 276:47623-47631, 2001; "Dimitroff"). This is respectfully traversed. The claims are directed to preparations of a substantially purified glycosylated CD44 polypeptide comprising an

amino acid sequence encoded by a nucleotide sequence comprising exons 1-5, 16, 18, and 20 of a human CD44 gene, wherein the CD44 polypeptide is a human CD44H isoform, a human CD44R1 isoform, or a human CD44R2 isoform, wherein the glycosylated CD44 polypeptide binds to an antibody having the binding specificity of monoclonal antibody HECA-452, and wherein the preparation comprises less than 30% of a polypeptide other than the glycosylated CD44 polypeptide.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. Sackstein does not describe a preparation comprising less than 30% of a polypeptide other than a glycosylated CD44 polypeptide including an amino acid sequence encoded by a nucleotide sequence comprising exons 1-5, 16, 18, and 20 of a human CD44 gene, wherein the CD44 polypeptide is a human CD44H isoform, a human CD44R1 isoform, or a human CD44R2 isoform. This element is missing from Sackstein and is not inherently present. Sackstein did not teach any substantially purified preparation of CD44, much less one comprising less than 30% of a polypeptide other than CD44. Such preparation is not "necessarily present" in Sackstein's disclosure, regardless of later-published characterizations of the work in Sackstein. Accordingly, withdrawal of the rejection of claims 1-7 and 62-63 as anticipated by Sackstein et al. is requested.

Stamenkovic et al.

Claims 1-7 and 62-63 were rejected as anticipated by Stamenkovic et al. (*EMBO J.*, 10:343-348, 1991; "Stamenkovic") as evidenced by Sackstein (U.S. Pat. Pub. No. 2003/0040607; "US 2003/0040607"). This is traversed.

As provided in the attached Declaration by Dr. Robert Sackstein, M.D., Ph.D. (hereafter referred to as "the Declaration"), the CD44 isoform disclosed by Stamenkovic is not the same as the claimed glycoprotein, referred to as HCELL. The CD44 isoform disclosed by Stamenkovic is not glycosylated and thus does not have the property of binding to an antibody having the specificity of monoclonal antibody HECA-452 as required by the claims. The Declaration explains that the cells used by Stamenkovic could not produce a CD44 isoform that is

Applicant : Robert Sackstein
Serial No. : 10/042,421
Filed : October 18, 2001
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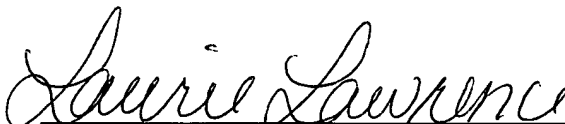
glycosylated such that it has the ability to bind an antibody having the specificity of monoclonal antibody HECA-452. Therefore, Stamenkovic does not teach or suggest every element of the claims, and thus, does not anticipate the claimed invention.

For the reasons provided above, Applicant respectfully requests that this rejection be withdrawn.

Enclosed is a check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 7/25/05


Laurie Butler Lawrence
Reg. No. 46,593

Fish & Richardson P.C.
225 Franklin St.
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (617) 542-8906



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Robert Sackstein Art Unit : 1644
Serial No. : 10/042,421 Examiner : Phillip Gambel
Filed : October 18, 2001
Title : HEMATOPOIETIC CELL E-SELECTIN/L-SELECTIN LIGAND
POLYPEPTIDES

MAIL STOP AF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF ROBERT SACKSTEIN, M.D., PhD UNDER 37 CFR §1.132

I, Robert Sackstein, M.D., PhD, pursuant to 37 C.F.R. § 1.132, declare the following:

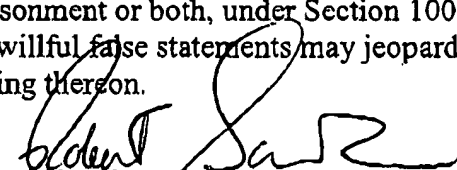
1. My educational and professional experience and qualifications are presented in the attached Curriculum Vitae (Appendix A).
2. I am the named inventor on the above-referenced United States Patent Application, No. 10/042,421.
3. I have reviewed the Office Action dated January 26, 2005 regarding the above-referenced application and understand that the Examiner has rejected the claims as anticipated by Stamenkovic et al. (1991) EMBO Journal 10:343-348 (referred to hereafter as "Stamenkovic"). In particular, it is my understanding that this rejection is based upon the Examiner's assertion that "given the teaching of the structural characterization (e.g. amino acid and encoding nucleic acids) of the CD44 isoforms as well as the hematopoietic source of said CD44 isoforms ..., the prior art appears to read on the claimed polypeptides."
4. Contrary to the Examiner's assertions, the CD44 isoform disclosed by Stamenkovic is not the same as the claimed glycoprotein, referred to as HCELL. While the CD44 peptide backbone of HCELL can be the same as the CD44 protein disclosed by Stamenkovic, HCELL is specialized glycosylated form of CD44 rendering a high affinity ligand for E-selectin or L-selectin and giving it the property of binding to an antibody having the specificity of monoclonal antibody HECA-452. The CD44 isoform disclosed by Stamenkovic does not have this property. Specifically, the CD44 isoform disclosed by Stamenkovic was produced by transfected COS cells and Namalwa cells. COS cells and Namalwa cells lack the glycosyltransferases necessary to modify CD44 to become a selectin ligand, i.e., the HCELL glycoform. Neither COS nor Namalwa cells express either CD15s nor HECA determinants. Moreover, COS are well-known to lack fucosyltransferase VII which is important for selectin ligand synthesis. Therefore, the CD44 isoform disclosed by Stamenkovic cannot be glycosylated such that it has the properties required by the claims, namely the ability to bind selectins and to be

recognized by a monoclonal antibody recognizing the relevant selectin-binding carbohydrate determinants (sialofucosylations), such as with the specificity of HECA 452.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

DATE:

July 22, 2005


Robert Sackstein, M.D., PhD.

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CURRICULUM VITAE

Name: Robert Sackstein, M.D., Ph.D.

Office Address: Harvard Institutes of Medicine
77 Ave. Louis Pasteur, Room 671, Boston, MA 02115
(phone: 617-525-5601)

Home Address: 26 Fox Run Road, Sudbury, MA 01776

E-mail: Rsackstein@rics.bwh.harvard.edu
Rsackstein@partners.org

FAX: 617-525-5571

Place of Birth: Havana, Cuba

Education:

1973-1977 A.B., *Summa Cum Laude*, Harvard College
1977-1985 M.D., Ph.D., Harvard Medical School

Postdoctoral Training:

1985-1986 Internal Medicine Internship, University of Miami/Jackson Memorial Hospital, Miami, FL
1986-1988 Internal Medicine Residency, University of Miami/Jackson Memorial Hospital, Miami, FL
1987-1989 Postdoctoral Fellowship in Immunology, University of Miami, Miami, FL
1989-1991 Hematology Training, University of Miami/Jackson Memorial Hospital, Miami, FL

Licensure and Certification:

1986 Florida Physician License
1989 Diplomate, American Board of Internal Medicine
1994 Diplomate, Subspecialty of Hematology
1997 Massachusetts Physician License

R. Sackstein, M.D.,Ph.D.

Academic Appointments:

1988-1989	Instructor of Medicine, University of Miami School of Medicine, Miami, FL
1989-1993	Assistant Professor of Medicine, Microbiology and Immunology, University of Miami School of Medicine, Miami, FL
1993-1996	Assistant Professor of Internal Medicine, Pathology and Laboratory Medicine, University of South Florida College of Medicine, Tampa, FL
1997-99	Assistant Professor of Surgery, Harvard Medical School, Boston, MA
1997-	Assistant Professor of Medicine, Harvard Medical School, Boston, MA
2002	Assistant Professor of Dermatology, Harvard Medical School, Boston, MA
2003-	Associate Professor of Dermatology and of Medicine, Harvard Medical School, Boston, MA

Hospital or Affiliated Institution Appointments:

1988-1989	Chief Medical Resident, Jackson Memorial Hospital, Miami, FL
1988-1993	Attending Physician, Emergency Room and Medical Services, Jackson Memorial Hospital, Miami, FL
1989-1993	Attending Physician, Medical Service, Miami Veterans Affairs Medical Center, Miami, FL
1991-1993	Attending Hematologist, Jackson Memorial Hospital and Miami VA Medical Center, Miami, FL
1991-1993	Director, Lymphoma Cutis Program, University of Miami NCI Comprehensive Cancer Center, Miami, FL
1993-1996	Attending Physician, Bone Marrow Transplant Service, and Director, Jenkins Foundation Transplant Immunology Research Laboratory, Moffitt Cancer Center and Research Institute, University of South Florida College of Medicine, Tampa, FL
1997-1998	Senior Investigator, Transplantation Biology Research Center, Massachusetts General Hospital, Boston, MA
1997-	Director, Translational Research Program, Bone Marrow Transplantation Unit, Hematology-Oncology Division, Department of Medicine, Massachusetts General Hospital, Boston, MA
1999-2002	Associate Physician, Brigham and Women's Hospital, Boston, MA
2002-	Physician, Brigham and Women's Hospital, Boston, MA

Other Professional Positions and Major Visiting Appointments:

1988-1989	Staff Physician, Metro-Dade County, Florida, Human Resources Health Center
1997	Visiting Scientist, Genetics Institute, Cambridge, MA

R. Sackstein, M.D.,Ph.D.

Hospital and Health Care Organization Service Responsibilities:

1988-1989 Chief Medical Resident, Jackson Memorial Hospital, Miami, FL
1993-1996 Director, Jenkins Foundation Transplant Immunology Research Laboratory and
Attending Physician, Bone Marrow Transplant Service, Moffitt Cancer Center and
Research Institute, University of South Florida College of Medicine, Tampa, FL

Major Administrative Responsibilities:

1990-1993 Faculty Director and Chairperson, Eastern Student Research Forum (an
international program to promote research by medical students)

Major Committee Assignments:

International:

1994- Scientific Advisory Committee to the Board of Trustees, Jose Carreras
International Leukemia Foundation (Fundacion Internacional Jose Carreras)

National:

1977-1985 Harvard Alumni Association, National Schools and Scholarship Committee and
National Recent Graduate's Committee
1990-1993 Faculty Director and Chairperson, Eastern Student Research Forum
1990-1993 National Council of American Federation for Clinical Research, University of
Miami Representative
1993-1997 National Council of American Federation for Medical Research, University of
South Florida Representative
1996- American Board of Internal Medicine Certification Examination, Subspecialty of
Hematology, Question Author
1999- Ad Hoc Reviewer, National Institutes of Health, Immunobiology Study Section,
Immunological Sciences Initial Review Group
2001- Member, NIH/NHLBI Working Group on Glycobiology
2000-2002 Co-ordinating Reviewer for Review Committee Category "Hematopoiesis: Stem
and Progenitor Cell Biology", American Society of Hematology Annual Meeting
2003 Ad Hoc Review, National Institutes of Health/NHLBI, Career Enhancement
Award Study Section
2004- Regular Member, Hematopoiesis (HP) Study Section, National Institutes of
Health/NHLBI

Regional:

1985-1993 Harvard Club of Miami, Schools and Scholarships Committee
1985-1993 Board of Directors, Miami Civic Music Association

R. Sackstein, M.D.,Ph.D.

- 1987-1993 Metro-Dade County (Florida), Advisory Board to County Homeless Health Care Project
- 1988-1989 Governor's Council, Florida Chapter of the American College Physicians
- 1991-1993 Dade County (Florida) School Board Planning Committee for Medicine and Allied Health Magnet School
- 1991-1993 Chairperson, Dade County School Board Subcommittees for Middle School Science Curriculum Review and for Community Outreach
- 1994-1995 Research Grant Peer Review Committee, American Heart Association, Florida Chapter
- 1994- Board of Directors, Museum of Science and Industry, Tampa, FL
- 1997- Member, Education Advisory Board, Discovery Museum, Acton, MA
- 2002 Harvard College 25th Reunion, Symposium Organizing Committee, Commencement Aid
- 2002- Harvard Club of Concord (MA), Schools and Scholarships Committee
- 2005- Reviewer, Fellowship Grants, King Trust/The Medical Foundation, Boston, MA

Medical School:

- 1987-1993 Admissions Committee, University of Miami School of Medicine Latin American Training Program
- 1998- Project Success Advisory Committee, Harvard Medical School
- 2000- Memorial Minutes Committee, Harvard Medical School
- 2003- Public Services Committee, The Countway Library of Medicine, Harvard Medical School
- 2004- Library Operations Subcommittee, The Countway Library of Medicine, Harvard Medical School

Hospital:

- 1987-1988 Executive Housestaff Committee, Jackson Memorial Hospital, Miami, FL
- 1989-1993 Miami VA Medical Center Subcommittees for the Research and Development Committee: Animal Experimentation Subcommittee; Chairperson, Equipment Subcommittee; Human Subjects Studies Subcommittee
- 1995-1996 Invasive Procedure and Blood Utilization Review Committee, H. Lee Moffitt Cancer Center and Research Institute
- 1996 Medical Staff By-Laws, Rules and Regulations Committee, H. Lee Moffitt Cancer Center and Research Institute
- 1997- Bone Marrow Transplant Protocol Review, Massachusetts General Hospital/Brigham and Women's Hospital/Dana-Farber Cancer Institute
- 2004- Steering Committee, MGH/BWH Departments of Dermatology, Joint Clinical Trials Unit

Professional Society Involvement:

- 1985- American Association for the Advancement of Science, member
- 1985-1997 American Federation for Clinical/Medical Research, member

R. Sackstein, M.D.,Ph.D.

1992- American Society of Hematology, member
1993-1997 International Society for Analytical Cytology, member
1993- International Society for Experimental Hematology, member
1993-1997 New York Academy of Sciences, member
2000- American Society of Clinical Oncology, member
2000- Abstract Reviewer, Annual Meeting of the American Society of Hematology
(Coordinating Reviewer for Category of "Hematopoiesis: Stem and Progenitor Cell Biology")

Community Service Related to Professional Work:

1987-1993 Volunteer Physician, Dade County Homeless Health Care Project
1987-1993 Member, Advisory Board, Dade County Homeless Health Care Project
1988-1989 Co-Medical Director (volunteer), Brothers of the Good Shepherd/Camillus House Health Concern (a free homeless health care clinic which I helped initiate)
1990-1993 Mentor, Laboratory Research Program (Dade County, FL, School System program for high school student lab research at regional colleges and universities)
1991-1993 Member, Dade County School Board Planning Committee for Medicine and Allied Health Magnet School (organized curriculum for magnet school)
1991-1993 Chairman, Dade County School Board Subcommittees for Middle School Science Curriculum Review and for Community Outreach
1992 Lead Judge, Dade County, Florida, Secondary School Science Fair
1992 Judge, Miami Herald Silver Knight Award, Science Category
1997 Non-Resident Tutor in Biology and Pre-Medical Studies, John Winthrop House, Harvard College
1994- Member, Board of Directors, Museum of Science and Industry, Tampa, FL
1998- Member, Education Advisory Board, Discovery Museum, Acton, MA
2001 Volunteer Physician, Pine Street Inn (Homeless Shelter), Boston, MA
2002 Organizer, Harvard College 25th Reunion Symposium on Biotechnology;
2002 Commencement Aid, Harvard University Commencement.
2002- Judge, Peter Noyes Elementary School Science Fair, Sudbury, MA

Awards and Honors:

1973-1977 John Harvard Scholarship (distinction awarded yearly for academic excellence), Harvard College
1974 Whittaker-Edwards Prize, Harvard College
1976 *Phi Beta Kappa*, Harvard College
1977 A.B., *Summa Cum Laude*, Harvard College (Baccalaureate in Biology, Thesis: "A Light Microscopic Study of Na⁺K⁺ATPase Activity in the Proximal Convulated Tubule of the Mammalian Kidney")
1977 Dr. Donald McKee Memorial Scholarship

R. Sackstein, M.D.,Ph.D.

- 1985 James Tolbert Shipley Prize for the "Best Research by a Student", Harvard Medical School
- 1989-1993 Veterans Affairs Research Career Development Award
- 1990 Recipient of "Kelly's Heroes Award" (for Community Service), WTVJ-TV (CBS), Miami, FL
- 1993 George Paff Award for Excellence in Teaching, University of Miami School of Medicine
- 1993 Stanley J. Glaser Foundation Award for "Outstanding Research Productivity and Achievement", University of Miami School of Medicine
- 1993 Recipient of the "Peace and Unity Award" (given by the Archdiocese of Miami for Community Service), Miami, FL
- 1996 New Investigator Award for Excellence in the Field of Hematology, International Society for Experimental Hematology

Part II: Report of Research:

A. Narrative Description of Research:

My efforts as a clinician and a basic scientist are intimately intermeshed. I am a basic science immunologist/biochemist/molecular biologist with clinical expertise in internal medicine/hematology/immunology and, in particular, in hematopoietic stem cell transplantation. Accordingly, my bench research efforts are directed at biologic processes critical to the survival of patients with cancer, especially those patients treated with high dose chemoradiotherapy and stem cell transplantation, such as: (1) tissue-specific lymphocyte migration (including the immunobiology of lymphocyte migration in pathologic reactions such as graft-versus-host disease), (2) hematopoiesis/stem cell biology, and (3) pathobiology of tumor cell proliferation and tumor metastasis. Lymphocytes recirculate continuously between vascular and tissue compartments, a process which is central to immunity in that it allows for the reassortment and distribution of appropriate lymphocyte effector cells for immune surveillance and immune responses. Lymphocyte migration is largely regulated by discrete lymphocyte-endothelial interactions within respective target tissues. The paradigm of tissue-specific lymphocyte migration is the trafficking of lymphocytes into peripheral lymph nodes, a process principally regulated by a lymphocyte membrane protein known as L-selectin which adheres to ligands expressed on lymph node high endothelial venules. In early work, our laboratory identified that L-selectin expression is characteristic not only of lymphocytes but also of early hematopoietic progenitor cells, and this observation led us to examine the expression of L-selectin ligands among bone marrow cells. These studies have identified an L-selectin ligand on early hematopoietic progenitor cells that is structurally distinct from L-selectin ligands expressed on endothelial cells. Subsequent biochemical studies from our laboratory revealed that this ligand, now known as Hematopoietic Cell E-/L-selectin Ligand (HCELL), is the most potent naturally-expressed E- and L-selectin ligand in the body. Though not recognized prior to this work, HCELL is not a "new" molecule – it is a specialized glycoform of CD44 expressed exclusively on hematopoietic stem cells. Through its role as a potent E-selectin ligand, HCELL may

function as the “bone marrow homing receptor” that directs stem cell migration into the marrow. Current studies are aimed at elucidating HCELL’s role in hematopoiesis and in the regulation of stem cell homing to bone marrow. In addition, HCELL is characteristically expressed on blasts of acute leukemia, and thus we are investigating how HCELL expression is related to leukemogenesis and how expression of this molecule is regulated on normal stem cells and leukemic blasts. More broadly, we are also studying the adhesion molecules that regulate homing of adult stem cells, in order to develop new strategies to improve the delivery of adult stem cells intravascularly to affected site(s) for tissue regeneration. In extension of these studies of “homing”, we are investigating the physiology of lymphocyte migration following stem cell transplantation, and have obtained evidence that the physiologic migration of lymphocytes to lymph nodes is disturbed in part because of disordered regulation of lymphocyte L-selectin gene expression. We are examining the molecular basis of altered L-selectin expression, and, moreover, we are studying how pathologic tissue-specific migration patterns develop post-transplant. In particular, acute graft-versus-host disease following allogeneic bone marrow transplantation is characterized by the directed migration of alloreactive lymphocytes into three principal target tissues - skin, liver and gut - wherein they mediate tissue destruction. Our laboratory has been examining the adhesion molecules that regulate skin-specific migration of lymphocytes in cutaneous GVHD reactions, in order to elucidate the molecular basis of this process and develop therapeutic agents to treat or prevent cutaneous GVHD. Our overall aim in these studies is to devise novel therapies to eliminate the detrimental GVHD reaction of allogeneic transplantation without disturbing beneficial immune reactions such as the graft-versus-malignancy effect. In other studies, we are investigating the structural biology of key molecules which mediate adhesive interactions that create microenvironmental “niches” for tumor cell proliferation, the adhesion molecules which allow for tumor cell dissemination, and the adhesion molecules that regulate lymphocyte trafficking to sites of tumor. The goal in these studies is to utilize structural information for the rational design of drugs that disrupt key adhesion molecules in tumor cell growth and metastasis, and that improve immune effector cell infiltration of tumor tissue.

B. Research Funding Information (only Principal and Co-principal Investigator Grants Listed):

1989-1993	Veterans Affairs Career Development Award, <u>Principal Investigator</u> , "Molecular Basis of Lymphocyte Migration"
1991-1993	Veterans Affairs Merit Grant, <u>Principal Investigator</u> , "Analysis of L-selectin Gene Expression in Thymocytes"
1992-1993	Stanley and Kathleen Glaser Research Foundation Grant, <u>Principal Investigator</u> , "Biology of L-selectin in Chronic Lymphocytic Leukemia"
1994-1995	American Cancer Society Research Grant (Florida Chapter), <u>Principal Investigator</u> , "L-selectin Ligand Expression in Bone Marrow Cells"
1993-1996	Jenkins Foundation Research Grant, <u>Principal Investigator</u> , "Lymphocyte Migration Following Bone Marrow Transplantation"
1997-2000	NIH/NHLBI, RO1, Co-Principal Investigator, "Compatibility of Swine Cells and Human Stroma"

R. Sackstein, M.D.,Ph.D.

- 1997-2002 NIH/NHLBI, RO1, Principal Investigator, “Molecular Analysis of Hematopoietic Cell L-selectin Ligand” (Competitively Renewed in 2002, see below, *renewal)
- 2001-2002 GlycoDesign, Inc., Principal Investigator, “Expression of HCELL on Normal Human Hematopoietic Cells” (\$125,000/year direct costs).
- 2001-2004 Elan Pharmaceuticals, Principal Investigator, “Cefepime as Monotherapy for Empiric Treatment of Febrile Neutropenia in BMT Recipients” (\$200,000 total costs).
- 2000-2005 NIH/NCI, RO1, Principal Investigator, “Adhesion Molecules Mediating Skin Tropism in Acute GVHD” (\$225,000/year direct costs).
- 2002-2007 NIH/NHLBI, RO1 (*renewal), Principal Investigator, “Structure and Biology of Hematopoietic Cell E-/L-selectin Ligand” (\$250,000/year direct costs).
- 2003-2007 NIH/NHLBI, RO1, Principal Investigator, “Analysis of Homing Receptors on Human Adult Stem Cells” (\$350,000/year direct costs).
- 2003-2008 NIH/NHLBI, R25, Co-principal Investigator, “Harvard Medical School MKITS Program” (\$200,000/year direct costs)

C. Report of Current Research Activities:

Hematopoietic and immunologic recovery following hematopoietic stem cell transplantation; physiology and molecular basis of lymphocyte and adult stem cell migration; structural biology and biochemistry of adhesion molecules; pathobiology of tumor metastasis; cancer therapeutics; pathobiology of graft-versus-host disease; treatment of infectious complications of bone marrow transplantation; use of adult stem cells for tissue regeneration.

R. Sackstein, M.D.,Ph.D.

D. Report of Teaching:

Local Contributions:

Harvard College

1976-1977 Natural Sciences 5, Teaching Assistant (introductory course for biology majors, Department of Biology); 20 students, 6 hours/wk, 2 terms

1975-1977 Tutor in Sciences, Harvard University Bureau of Study Council

Harvard Medical School

1979 Physiology and Biophysics 700.0, Teaching Assistant (first-year physiology course); 110 students, 5 hours/wk, 4 weeks

1998 GSAS Program in Biological and Biomedical Sciences
Doctoral Thesis Examining Committee (Dr. Erik Finger)

2001 Reader and Examiner, HMS M.D. Honors Thesis Program (Anna Chapas)

1999- Course Lecturer, HST Hematology (HST-080)
25 students, 2 hours lecture, 20 hours/year

2001- Preceptor, Introduction to Clinical Medicine, HST Program (at the BWH)
Assigned 2 students, 100 hours/year (full-time preceptor)

University of Miami School of Medicine

1985-1992 Core Immunobiology Course, Laboratory and Conference Instructor; 150 students, 4 hours/week, 3 weeks

1988-1992 Physical Diagnosis Course, Instructor (second-year students); 3 students/year, 5 hours/week, one term/year

1990 "Life Cycle" Module, Physician - Scientist Program, Tutor; 7 M.D., Ph.D. students in tutorial, 10 hours/week, 8 weeks

1992 "Autoimmune Disease", Course Director, (Microbiology and Immunology Department Graduate Level course); 5 graduate students, 15 hours/week, 5 weeks

University of South Florida College of Medicine

1993-1994 Physical Diagnosis, Instructor; 2 students, 5 hours/week, one term/year

R. Sackstein, M.D.,Ph.D.

1993-1996 Medical Microbiology and Immunology Course (1993-96) and Hematology Course (1996), Course Lecturer; each course, 130 medical students, 2 lectures in each course, 20 hours/year

Advisory and Supervisory Responsibilities:

Laboratory Supervision (students/fellows): University of Miami (1989-1993): lab supervisor/advisor to high school students in the Secondary School Laboratory Research Program and to three college students

University of South Florida (1993-1996): lab supervisor/advisor to two college students and three graduate students.

Postdoctoral fellow trainees are as follows:

Lou Meng, M.D., University of Miami, 1990-1993. Was *Assistant Professor of Pathology*, University of Miami School of Medicine (1993-2000); now working in industry.

Jane Messina, M.D., University of South Florida, 1993-1995. Now *Associate Professor of Pathology*, University of South Florida College of Medicine.

Katrina Allen, Ph.D., University of South Florida, 1993-96. Now stay-at-home mother.

Khizuang Shu, M.D., Postdoctoral Fellow, University of South Florida, 1994-96. Now working in industry.

Han Chong Toh, M.D.,Ph.D., Postdoctoral Fellow, Massachusetts General Hospital, 1997-99. Now a practicing *academic physician in Singapore*.

Sanhita Rakshit, Ph.D., Post-doctoral Fellow, Harvard Institutes of Medicine/Brigham and Women's Hospital, 2001-2002; now working in industry.

Onir Leshem, DDS, Post-doctoral Fellow, Harvard Institutes of Medicine/Brigham and Women's Hospital, 2001-2002. Now pursuing a Ph.D. at Forsythe Dental Center, Boston, MA.

Charles J. Dimitroff, Ph.D., Post-Doctoral Fellow, Harvard Institutes of Medicine/Brigham and Women's Hospital, 1999-2003. Now *Instructor of Dermatology*, Harvard Medical School.

Mirjana Milinkovic, M.D., Post-doctoral Fellow, Harvard Institutes of Medicine/Brigham and Women's Hospital, 2001-2003. Now *Assistant Professor of Dermatology*, University of Belgrade, Serbia.

R. Sackstein, M.D.,Ph.D.

Min Xu, M.D., Post-doctoral Fellow, Harvard Institutes of Medicine/Brigham and Women's Hospital, 2002-2004. Now a Surgical Resident, Tufts Medical Center.

Monica Burdick, Ph.D., Post-doctoral Fellow, Harvard Institutes of Medicine/Brigham and Women's Hospital, 2003- present

Jennifer Bracy, Ph.D., Post-doctoral Fellow, Harvard Institutes of Medicine/Brigham and Women's Hospital, 2003-2004

Nilesh Dagia, Ph.D. Post-doctoral Fellow, Harvard Institutes of Medicine/Brigham and Women's Hospital, 2004-present

Zeineb Gadhoum, Ph.D., Post-doctoral Fellow, Harvard Institutes of Medicine/Brigham and Women's Hospital, 2004-present

Bianling Liu, M.D., Post-doctoral Fellow, Harvard Institutes of Medicine/Brigham and Women's Hospital, 2004-present

Vicente Resto, M.D., Ph.D., Post-doctoral Fellow, Harvard Institutes of Medicine/Brigham and Women's Hospital, 2004-present

Ons Samih Al-Khadra, Ph.D. Student (Harvard Dental School), 2004-present

Julia T. Chu, HST Student (independent research), 2004-present

John Adler, III, Harvard Undergraduate (performing independent research towards thesis (91R)), 2004-present

Regional, National or International Contributions:

Invited Presentations:

- | | |
|------|---|
| 1983 | Plenary Session Speaker, International Complement Workshop, Mainz, Germany, "Phylogenetic Conservation of the MHC Protein Factor B" |
| 1984 | Seminar Chairperson and Speaker, Harvard Medical Society Symposium, "Effector Functions of the Macrophage" |

R. Sackstein, M.D.,Ph.D.

- 1985 Speaker, Harvard Medical School, Department of Pathology, "The Complement Genes of the Major Histocompatibility Complex"
- 1986 Speaker, Department of Immunology and Microbiology Seminar Series, University of Miami School of Medicine, "The Class III Genes of the MHC"
Keynote address, Greater Miami Interdenominational Faith Conference, "Acquired Immunodeficiency Disease"
Lecturer, Temple Israel Miami Health Symposium, "The Current Truth About AIDS"
- 1987 Speaker, Dade County Family Services Center, "AIDS: The Facts".
- 1988 Plenary Session Speaker, Annual Meeting, Florida Division of American College of Physicians, "Health Care and the Homeless"
- 1990 Speaker, Department of Immunology and Microbiology Seminar Series, University of Miami School of Medicine, "Lymphocyte Migration"
- 1991 Speaker, University of Miami School of Medicine, Medical Grand Rounds, "Chronic Lymphocytic Leukemia"
- 1992 Speaker, H. Lee Moffitt Cancer Center Grand Rounds, University of South Florida, "Lymphocyte Homing Receptors"
Plenary Session Speaker, Annual Meeting, Leukemia Society of South Florida, "Immunobiology of Chronic Lymphocytic Leukemia"
Plenary Session Speaker, International Congress of Cuban Physicians, "Immunobiology of Lymphoma and Leukemia"
Speaker, Department of Immunology and Microbiology Seminar Series, University of Miami School of Medicine, "The Effects of Steroids on Lymphocyte Migration"
- 1993 Speaker, University of South Florida Department of Pathology and Laboratory Medicine Grand Rounds, "Pathophysiology of Lymphocyte Migration"
- 1994 Speaker, NIH/NHLBI; Hematology Branch, Invited Seminar Series, "Lymphocyte Migration: The Biology of L-Selectin"
Speaker, University of South Florida Department of Medicine Grand Rounds, "Lymphocyte Migration in Health and Disease"
Speaker, University of South Florida Department of Biochemistry and Molecular Biology Seminar Series, "Regulation of L-selectin Gene Expression"
Speaker, Fred Hutchinson Cancer Center Seminar Series, University of Washington, "The Physiology of Lymphocyte Migration Following Bone Marrow Transplantation"

- 1995 Plenary Session Speaker, New York Academy of Sciences Conference on Bone Marrow Transplantation, "Lymphocyte Migration Following Bone Marrow Transplantation"
Speaker, Gibco-BRL/Life Technologies, Bethesda, MD, "Expression of an L-Selectin Ligand on Hematopoietic Progenitor Cells"
Speaker, Monsanto/Searle/Washington University Immunology Seminar Series, "The Biology of L-Selectin Ligands"
Speaker, Harvard Medical School, Hematology/Oncology Grand Rounds, Brigham and Women's Hospital/Beth Israel Hospital, "Adhesion Molecules and Hematopoiesis: Is CD34 an L-Selectin Ligand?"
Speaker, Harvard Medical School/Beth Israel Hospital, Department of Pathology, "Tissue-Specific Lymphocyte Migration Following Bone Marrow Transplantation"
Speaker, University of South Carolina School of Medicine, Hematology/Oncology Teaching Conference, "Pathophysiology of Lymphocyte Migration following Bone Marrow Transplantation"
Speaker, University of South Florida Department of Pathology and Laboratory Medicine Grand Rounds, "The Biology of Selectins: Mediators of the Inflammatory Response"
Speaker, Visiting Scientist Lecture Series, Genetics Institute, Cambridge, MA, "Structural Biology of L-selectin Ligands"
- 1996 Speaker, Gene Therapy Laboratories Seminar Series, University of Southern California, "L-Selectin Ligand as a Target for Gene Therapy"
Plenary Session Speaker, Keystone Symposium on the Hematopoietic Microenvironment, Taos, NM, "The Hematopoietic Microenvironment: The Biology of L-Selectin"
Speaker, City of Hope National Cancer Center, Duarte, CA, "The Biology of L-Selectin and its Ligands in Hematopoiesis", and "The Pathophysiology of Lymphocyte Migration in GVHD"
Speaker, Jose Carreras International Leukemia Foundation Scientific Symposium, Barcelona, Spain, "The Biology of L-Selectin in Hematolymphopoiesis"
Speaker, Hematology/Oncology Division, University of Murcia School of Medicine, Murcia, Spain, "Lymphocyte Migration to Target Tissues in GVHD"
Speaker, Mayo Cancer Center Forum on Hematopoietic Stem Cells, Mayo Clinic, Rochester, MN, "The Biology of L-Selectin in Hematolymphopoiesis"
Speaker, University of Virginia School of Medicine, Hematology/Oncology Grand Rounds, "Adhesion Molecules and Hematopoiesis"
Plenary Session Speaker (Presidential Symposium), 25th Anniversary Meeting of the International Society for Experimental Hematology, "A Novel L-selectin Ligand is Expressed on Normal Human Hematopoietic Cells"
Speaker, Duke University Hematology/Bone Marrow Transplant Service Grand Rounds, "The Selectins and Their Ligands"

- 1997 Speaker, University of Pittsburgh Hematology/Bone Marrow Transplant Seminar Series, "Selectins and the Hematopoietic Microenvironment"
Speaker, Case Western Reserve University Cancer Center, Hematology/Oncology Division Seminar Series, "Graft-versus-Host Disease"
- 1998 Speaker, Harvard Skin Disease Research Center Seminar Series, "Pathobiology of Cutaneous GVHD"
Speaker, National Institutes of Health/National Heart, Lung, Blood Institute, Hematopoietic Stem Cell Biology Meeting, "Characterization of a Novel L-selectin Ligand Expressed on Hematopoietic Progenitor Cells"
Speaker, Pathology Research Seminar Series, Massachusetts General Hospital, "The Selectins"
- 1999 Speaker, Harvard Institutes of Medicine Immunology Seminar Series, "The Structural Biology of the L-selectin Ligands"
Speaker, Gastroenterology Grand Rounds, Massachusetts General Hospital, "GI Complications of Bone Marrow Transplantation"
Keynote Banquet Speaker, Eastern Student Research Forum (University of Miami), "The Making of a Translationalist"
Speaker, Boston Glycobiology Discussion Group, "The Glycobiology of the Selectin Ligands"
Speaker, Bone Marrow Transplant Conference, Dana-Farber Cancer Institute, "Site-specific Migration of Lymphocytes in Graft-versus-Host Disease"
- 2000 Speaker, Roswell Park Cancer Institute, Department of Pharmacology and Developmental Therapeutics Seminar Series, "Characterization and Structural Biology of HCLL, A Novel L-selectin Ligand"
Speaker, Roswell Park Cancer Institute Medical Grand Rounds, "Biology and Pathobiology of Lymphocyte Migration"
Speaker, Tulane University Cancer Center Seminar Series, "Leukocytes and the Mississippi: Rollin' Along"
Speaker, Hennepin County Medical Center/University of Minnesota, Nephrology/Renal Transplant Program Seminar Series, "The Molecular Basis of Tissue-specific Lymphocyte Migration"
Speaker, University of Minnesota Cancer Center, Bone Marrow Transplant Grand Rounds, "Pathobiology of Lymphocyte Migration in Acute GVHD"
Speaker, Vascular Biology Research Conference, Department of Pathology, Brigham and Women's Hospital, "The Development of the 'Blot Rolling Assay'"
- 2001 Keynote Speaker, Eastern Student Research Forum (University of Miami), "The Intern Asked the Question: So, How is it that Blood Cells Migrate into the Bone Marrow?"
Keynote Speaker, Southern New England Junior Science and Humanities Symposium, "How is a Scientist 'Made'?"

Speaker, University of Washington Hematology/Oncology Grand Rounds, “Shear Madness: How Hematopoietic Cells Home to Bone Marrow”

Speaker, National Institutes of Health/National Heart, Lung, Blood Institute, Hematopoietic Stem Cell Biology Meeting, “Development and Use of the ‘Blot Rolling Assay’ to Identify a Novel Selectin Ligand Expressed on Hematopoietic Progenitor Cells”

Speaker, Oregon Health Science University Cancer Center, “Novel Methods to Improve the Clinical Diagnosis and Management of Acute Graft-versus-Host Disease”

Speaker, Bone Marrow Transplant Conference, Dana-Farber Cancer Institute, “The Migration of Stem Cells into Bone Marrow”

Speaker, Chief Medical Resident’s Teaching Conference, Brigham and Women’s Hospital, “The Science and Politics of Embryonic and Adult Stem Cell Research”

Speaker, Harvard Medical School, Vascular Biology Seminar Series, “Hermes, HCELL and Hematopoiesis: Homing in on CD44”

Honorary Speaker, Dr. Larry M. Fishman Symposium, University of Miami School of Medicine, “Adult Stem Cells: Politics, Plasticity and Promise for the Future”

2002 Speaker, MGH Cancer Seminar Series, “The ‘Roll’ of Selectins: How Stem Cells Migrate”

Speaker, 3rd International Workshop on Non-myeloablative Stem Cell Transplantation (Captiva Island, FL), “Novel Methods of Diagnosing Graft-versus-Host Disease”

Speaker, Roger Williams Hospital Cancer Center Seminar Series, “How Stem Cells Learn to ‘Crawl’”

Moderator and Speaker, Harvard College Class of 1977 (25th Reunion) Reunion Symposia, Symposium on Biotechnology, “Stem Cell Therapies: Do We Need Embryonic Stem Cells to Treat Disease?”

Speaker, Bone Marrow Transplant Conference, Dana-Farber Cancer Institute, “The Pathobiology of Acute GVHD: A Double-edged Sword”

2003 Speaker, 4th International Workshop on Non-myeloablative Stem Cell Transplantation (Bermuda), “Strategies to Enhance Lymphocyte Migration to Sites of Relapse Following Non-myeloablative Stem Cell Transplantation”

Speaker, Center for Blood Research Seminar Series, Harvard Medical School, “Human Hematopoiesis: Homing in on CD44”

Speaker, New England Regional Primate Center, Harvard Medical School, “The Peripatetic Adult Stem Cell”

Speaker, 52nd Annual Montagna Symposium on the Biology of Skin, “The Trafficking of Adult Stem Cells”

Speaker, Bone Marrow Transplant Conference, Dana-Farber Cancer Institute, “Optimizing Homing of Hematopoietic Stem Cells for Regenerative Therapies”

Speaker, Johns Hopkins Department of Pharmacology Seminar Series, “The Discovery of ‘HCELL’, the Bone Marrow ‘Homing Receptor’”

- Plenary Speaker, Hyaluronan 2003 (International Conference), “The ‘Roll’ of Hyaluronic Acid in Acute Cutaneous Graft-versus-Host Disease”
Speaker, Connecticut Society of Dermatology and Dermatologic Surgery Annual Meeting, “Recent Advances in Our Understanding of Acute Cutaneous GVHD”
Speaker, Immunology Seminar Series, All-Children’s Hospital, St. Petersburg, FL, “The Molecular Basis of Acute GVHD”
Speaker, Grand Rounds, All-Children’s Hospital, St. Petersburg, FL, “New ‘Avenues’ in Medicine: Hematopoietic Stem Cells and Regenerative Therapies”
- 2004 Speaker, University of Miami, Medical Grand Rounds, Miami, FL, “Regenerative Medicine: Implications for Future Clinical Management”
Speaker, Satellite Symposium, Annual Meeting of the American Society of Blood Marrow Transplantation, Orlando, FL, “T Cell Depletion and Leukocyte-Endothelial Interactions in Hematopoietic Stem Cell Transplantation”
Speaker, Cleveland Clinic Immunology Seminar Series, Cleveland Clinic Foundation, Cleveland, OH, “Subverting the Inflammatory Response for Regenerative Medicine”
Speaker, International Meeting of the Society of Glycobiology (combined with Japanese Society of Carbohydrate Research, Honolulu, HI, “From Graft Failure to Graft-versus-Host Disease: The Central Role of Glycans in Allogeneic Bone Marrow Transplantation”
- 2005 Speaker, 5th International Workshop on Non-myeloablative Stem Cell Transplantation (Cancun, Mexico), “Physiology and Pathobiology of Lymphocyte and Stem Cell Migration”
Speaker, Bone Marrow Transplant Conference, Dana-Farber Cancer Institute, “Strategies to Enhance Lymphocyte Migration to Sites of Relapse Following Hematopoietic Stem Cell Transplantation”
Speaker, Boston Glycobiology Discussion Group, “The Role of Glycans in Stem Cell Migration”

E. Report of Clinical Activities:

Clinical Practice: Bone marrow transplantation, hematology and internal medicine, teaching hospital

Time Commitments: Patient care 25%, teaching 10%, administration 5%, research 60% (community service is performed outside of work environment and comprises 10% commitment)

Patient Load: Predominantly in-patient, with emergency out-patient evaluation and treatment

Clinical contributions: All clinical efforts in bone marrow transplantation are research-based to improve patient treatments/outcomes

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Original Reports:

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2. Sackstein R, Colten HR. Molecular regulation of MHC class III (C4 and factor B) gene expression in mouse peritoneal macrophages. *J. Immunol.* 1984; 133:1618-1626.
3. Chaplin DD, Sackstein R, Perlmutter DH, Weis JH, Kruse TA, Coligan J, Colten HR, Seidman JG. Expression of hemolytically active murine fourth component of complement in transfected L cells. *Cell* 1984; 37:569-576.
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- transplantation for multiple myeloma with end stage renal disease: The induction of allograft tolerance through mixed lymphohematopoietic chimerism. *Transplantation* 1999, 68: 480-484.
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R. Sackstein, M.D.,Ph.D.

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